

Partnerships to Improve Immunotoxicity Testing

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Research in ITB is focused on the effects that chemicals/environmental contaminants have on modulation of the immune system. Immune modulation may result in suppressed immune function, while exposure to certain contaminants may result in hypersensitivity reactions (e.g., asthma or cutaneous inflammation). In order for the office of Prevention, Pesticides and Toxic Substances to identify and determine the potential of chemicals, regulated under the Toxic Substances Control Act and the Federal Insecticide, Fungicide and Rodenticide Act, to suppress or induce immune function, the development and validation of sensitive and predictive immune system assays is critical. ITB has and is involved in collaborations with government, industry, and academic laboratories, addressing issues related to the sensitivity of the immune endpoints used to detect immunosuppression and hypersensitivity. Partnerships between ITB and other laboratories include the following: A. Evaluation of cytokine mRNA profiles for the potential to aid in identification of airway sensitizers with two industry labs. The data demonstrated diverse responses of different low-molecular-weight chemicals, which suggest the need to definitively link these differences in immune responses to differences in respiratory responses. B. Participated with eight academic and government labs, plus six industry labs, in an international program on chemical safety study in rats, comparing the sensitivity of immune function assays versus histopathology following immunosuppression by azathioprine or cyclosporin. The antibody response and the performance of “enhanced pathology” each appeared to identify immunosuppression at relatively comparable doses. C. The evaluation and identification of the sensitivity of two antibody response assays for routine immunotoxicity testing, which involved two industry labs and one academic lab. The results revealed that the antibody-producing plaque-forming cells (PFC) assay was more sensitive than serum antibody titers. D. Participated in a series of studies in conjunction with the National Toxicology Program, National Institute of Environmental Health Sciences, and the NHEERL Neurotoxicology Division, focusing on examination of the effects that pesticides have on the developing rats’ reproductive, immune, and central nervous systems. Perinatal exposure to heptachlor and methoxychlor resulted in immunosuppression in the adult rats. E. Participated in collaborations with the International Life Sciences Institute in organizing immunotoxicology workshops on respiratory hypersensitivity and developmental immunotoxicity, plus a potential workshop on allergenicity of biotechnology products. F. We are presently supported by the American Chemistry Council to perform studies to determine the susceptibility of the developing immune system to known immunosuppressants. G. We are organizing a workshop on practical genomics and immunotoxicity for September. (This poster does not reflect the U.S Environmental Protection Agency policy.)